BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-020923
Article Type:	Research
Date Submitted by the Author:	02-Dec-2017
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Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Health policy
Keywords:	PRIMARY CARE, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Paediatric infectious disease & immunisation < PAEDIATRICS, PREVENTIVE MEDICINE, PUBLIC HEALTH

TITLE PAGE

Public subsidies and the recommendation of child vaccines among primary care physicians: a nationwide study in Japan

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Word count: 2,537 words

ABSTRACT

Objectives

Although public subsidies and physician recommendations for vaccination play key roles in increasing childhood vaccination coverage, the association between them remains uncertain. This study aimed to identify the association between awareness of public subsidies and recommendations for *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (PCV), and human papillomavirus (HPV) vaccinations, among primary care physicians in Japan.

Design

Cross-sectional study

Setting

In 2012, a questionnaire was distributed among 3,000 randomly selected physicians who were members of the Japan Primary Care Association.

Participants

From the questionnaire, participants were limited to physicians who administered childhood vaccinations.

Primary and Secondary Outcome Measures

The primary measures were participants' awareness of public subsidies and their recommendation levels for Hib, PCV, and HPV vaccines. Multiple logistic regression analysis was performed to investigate the

association between awareness and recommendation, with adjustment for possible confounders.

Results

Of 743 physician respondents, 434 were included as analysis subjects. The proportions that recommended vaccinations were 57.1% for Hib, 54.2% for PCV, and 58.1% for HPV. For each vaccine, multivariable analyses showed physicians who were aware of the subsidy were more likely to recommend vaccination than those who were not aware: the adjusted odds ratios were 4.21 (95% confidence interval [CI] 2.47–7.15) for Hib, 4.96 (95% CI 2.89–8.53) for PCV, and 4.17 (95% CI 2.00–8.70) for HPV.

Conclusions

Primary care physicians' awareness of public subsidies was found to be associated with their recommendations for the Hib, PCV, and HPV vaccines. Provision of information about public subsidies to these physicians may increase their likelihood to recommend vaccination.

Strengths and limitations of this study

- This is the first study to focus on the association between awareness of primary care physicians (PCPs) concerning vaccination subsidies and those PCPs' recommendations for vaccinations for children.
- Through multivariable analysis, we explored characteristics of PCPs who were associated with less vaccination recommendation; this may provide important information on how to increase such recommendations and vaccination coverage.
- One limitation was the low response rate, which may have caused non-responder bias.
- Another limitation was that the results' generalizability for PCPs outside of Japan was unclear.

MAIN TEXT

Introduction

Vaccination has proven to be a successful and cost-effective health intervention in preventive care.[1] Vaccination against *Haemophilus influenzae* type b (Hib) is a successful example. In the United States, introduction of the Hib vaccine reduced incidence of invasive Hib disease by 99%,[2] while in Kenya, a 93% decline was seen following vaccination.[3] Therefore, many childhood vaccines (including Hib) are routinely provided, especially in higher-income countries, where coverage is relatively high.[4-8]

In Japan, however, many important vaccines, including Hib, *Streptococcus pneumoniae* (7-valent pneumococcal conjugate vaccine: PCV), and human papillomavirus (HPV) are voluntary rather than routine. Without public subsidies, patients must pay an out-of-pocket fee, and this cost burden may serve as a barrier to receiving vaccination.[9] Coverage of traditional, routine vaccinations (e.g., those for diphtheria, tetanus, and measles) is high, and their associated diseases are well-controlled.[9-11] However, coverage of voluntary vaccinations is much lower.[9] The Hib vaccine, for example, was first introduced to Japan in 2008 on a voluntary basis, and had estimated coverage of 5%–10% in 2010.[12] Therefore, the Government of Japan implemented subsidies for local governments for Hib, PCV, and HPV vaccine fees from November 2010.[13] All local governments have now started providing public subsidies for these three vaccines.

It is generally accepted that recommendation of vaccination, to children and their parents by a physician, is important for increasing coverage.[13-17] Primary care physicians (PCPs) provide care for all ages, from children to older people, and play a key role in childhood vaccination as vaccine providers, as well as pediatricians. However, no previous studies have examined PCPs' level of awareness of public subsidies for childhood vaccines in Japan, and the association between this awareness and recommendations for vaccination. Therefore, this study aimed to examine this association among PCPs in Japan for the Hib, PCV, and HPV vaccinations.

Methods

Study design, setting, and population

This study used a cross-sectional design with data drawn from a questionnaire conducted by the Japan Primary Care Association (JPCA), the largest academic association for PCPs in Japan. The survey was conducted in September–November 2012. In total, 3,000 physicians were randomly selected from among the 5,977 JPCA physician members. Selection was made using a random number list. Subject participants were then selected from among these 3,000 physicians in accordance with inclusion and exclusion criteria. The inclusion criteria were: physicians who were JPCA members and who administered childhood vaccination (defined as those who administered at least one of the Hib, PCV, and HPV vaccines in daily medical practice). Exclusion criteria were physicians who were retired or within

2 years of their postgraduate year (PGY), as the latter group are classified as "junior residents" in Japan. Questionnaire items were based on previous studies.[14 15 17-26] We used a self-administered, anonymous questionnaire design and collected data on the participating PCPs' main practice category, practice setting (clinic, hospital, or other), local government of the practice, population under jurisdiction of the local government, and experience as a kindergarten or other school physician. Additional details are given below.

Main exposure

The main exposure of this study was physicians' awareness of the existence of local government public subsidies for the target vaccine (awareness of public subsidy). For each vaccine, respondents were asked "Does the local government of your place of practice subsidize the vaccination?" Response options were "Yes," "No," and "I don't know." Answers of "Yes" were defined as "awareness of public subsidy." Answers of "No" or "I don't know" were defined as "no awareness of public subsidy."

Main outcome

The main outcome of this study was PCPs' active recommendation of a target vaccine to children and the children's parents in daily medical practice ("recommendation"). For each vaccine, respondents were asked "How do you recommend a target vaccine to vaccinees and their parents?" Response options, on a

Likert-type scale, were: “Always recommend,” “Maybe recommend,” “No opinion,” “Not recommend actively,” and “Not recommend.” Answers of “Always recommend” were defined as “recommendation.” “Maybe recommend,” “No opinion,” “Not recommend actively,” and “Not recommend” were defined as “no recommendation.”

Possible confounders

Possible confounders were the physician’s sex, PGY, a proportion of pediatric patients (pediatric patients in the total patient population) that was high (≥10%) or low (<10%), and experience raising children as a parent. We added in these data from the questionnaire and also used public information held by the local government to investigate the type of the subsidy (full subsidy or not) for the three vaccines for each participant.

Statistical analyses

Logistic regression analysis was performed for each target vaccine (Hib, PCV, and HPV) to investigate the association between PCPs’ awareness of a public subsidy for the target vaccine and their recommendation of that vaccine. Then, multiple logistic regression analysis was performed to investigate the association between awareness and recommendation, adjusting for possible confounders (full subsidy or not, physician’s sex, PGY, proportion of pediatric patients, and experience raising

children).

The analysis subjects were set after excluding participants with missing data for the main exposure, main outcome, and possible confounders (mentioned above).

All statistical analyses used two-tailed tests of significance, with significance set at 0.05. Analyses were performed with Stata/SE 13.1 (StataCorp LLC, College Station, TX, USA). Sensitivity analysis was performed for each vaccine using another method of re-categorization to reflect the dichotomization of the dependent variable (recommendation), with the response option "Maybe recommend" included in "recommendation."

We obtained written informed consent from all participants before we conducted the survey. The study protocol was approved by the Institutional Review Board of Saga University Hospital (2012-05-13) and the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (E2528).

Results

Study flow and demographics

Of the 3,000 randomly selected PCPs, 120 were excluded based on the inclusion and exclusion criteria, leaving a sample of 2,880. We received responses from 743 PCPs, for a response rate of 25.8%. Of these, 480 (64.6%) administered childhood vaccinations. We analyzed data for 434 (58.4%) after excluding 46

(9.6%) with missing data for covariates (Figure 1). The majority of these PCPs were men, PGY 11–40, reported a clinical category of primary care, reported their practice setting as clinic, and had experience raising children (Table 1).

Table 1. Participants' characteristics

Characteristic	Analysis subjects n=434 n (%)	Responders n=743 n (%)	All physician members† n=5,939 n (%)
Gender: male	367 (84.6)	624 (84.0)	5,071 (85.4)
Postgraduate year：3-10	90 (20.7)	153 (20.6)	664 (11.7)
11-40	318 (73.3)	527 (71.0)	4248 (74.8)
>=41	26 (6.0)	62 (8.4)	769 (13.5)
Main practice category: primary care	358 (82.5)	556 (74.8)	-
Practice setting; clinic	307 (70.7)	388 (52.3)	-
Pediatric patients >=10%	174 (40.1)	186 (26.2)	-
Population of local government >= 50,000	277 (64.0)	527 (71.5)	-
Experience of kindergarten or other school physician	284 (65.4)	403 (54.2)	-
Experience raising children	343 (79.0)	568 (76.5)	-

†Physician members of the Japan Primary Care Association as of September 2012.

Main practice category: primary care: Answered main practice category as family physician or general practitioner or hospitalist/general physician; Pediatric patients: proportion of pediatric patients in the total patient population.

Hib vaccine

Characteristics of PCPs were stratified by recommendation of the Hib vaccine and the association between awareness of an Hib vaccine public subsidy and vaccination recommendation (Table 2). We found 327 (75.3%) PCPs reported awareness of a public subsidy and 248 (57.1%) recommended the vaccine. PCPs who reported awareness were significantly more likely to recommend the vaccine than those who were not aware (non-adjusted analysis: OR 6.18, 95% confidence interval [CI] 3.77–10.12, $p<0.001$; multivariable analysis: adjusted odds ratio [AOR] 4.21, 95% CI 2.47–7.15, $p<0.001$). A higher proportion of pediatric patients and of PCPs with experience raising children were positively associated with recommendation. However, a higher PGY number was inversely associated (Table 3).

Table 2. Primary care physicians' awareness of public subsidies and recommendation levels for the *Haemophilus influenzae* type b vaccine, 7-valent pneumococcal conjugate vaccine, and human papillomavirus vaccine

n=434

Awareness of public subsidy for each vaccine	Recommendation level for each vaccine, n (%)					
	Always Recommend	Maybe Recommend	No opinion	Not recommend actively	Not Recommend	Total
Hib vaccine						
Awareness (+)	221 (50.9)	78 (18.0)	23 (5.3)	3 (0.7)	2 (0.5)	327 (75.3)
Awareness (-)	27 (6.2)	40 (9.2)	27 (6.2)	8 (1.8)	5 (1.2)	107 (24.7)
Total	248 (57.1)	118 (27.2)	50 (11.5)	11 (2.5)	7 (1.6)	434 (100)
PCV vaccine						
Awareness (+)	211 (48.6)	77 (17.7)	22 (5.1)	4 (0.9)	1 (0.2)	314 (72.4)
Awareness (-)	24 (5.5)	45 (10.4)	36 (8.3)	8 (1.8)	6 (1.4)	119 (27.4)
Total	235 (54.2)	122 (28.1)	58 (13.4)	12 (2.8)	7 (1.6)	434 (100)
HPV vaccine						
Awareness (+)	241 (55.5)	121 (27.9)	19 (4.4)	6 (1.4)	2 (0.5)	389 (89.6)
Awareness (-)	11 (2.5)	18 (4.1)	13 (3.0)	3 (0.7)	0 (0)	45 (10.4)
Total	252 (58.1)	139 (32.0)	32 (7.4)	9 (2.1)	2 (0.5)	434 (100)

Hib: *Haemophilus influenzae* type b; PCV: 7-valent pneumococcal conjugate vaccine; HPV: human papillomavirus.

Table 3. Association between primary care physicians' characteristics and recommendation of *Haemophilus influenzae* type b vaccine

n=434

Variable	Recommendation for Hib vaccine, n (%)			Non-adjusted analysis			Multivariable analysis		
	Total, n=434	Recommen-dation (+), n=248	Recommen-dation (-), n=186	OR	95% CI	p value	AOR	95% CI	p value
Awareness of public subsidy for Hib vaccine	327 (75.4)	221 (89.1)	106 (57.0)	6.18	3.77 - 10.12	<0.001	4.21	2.47 - 7.15	<0.001
Full subsidy	371 (85.5)	209 (84.3)	162 (87.1)	-	-	-	0.76	0.41 - 1.41	0.39
Male	367 (84.6)	205 (82.7)	162 (87.1)	-	-	-	0.97	0.52 - 1.80	0.93
Postgraduate year：3-10	90 (20.7)	68 (27.4)	22 (11.8)	-	-	-	Ref.		
11-40	318 (73.3)	168 (67.7)	150 (80.6)	-	-	-	0.32	0.17 - 0.61	<0.001
>=41	26 (6.0)	12 (4.8)	14 (7.5)	-	-	-	0.19	0.07 - 0.53	0.001
Pediatric patients >=10%	174 (40.1)	127 (51.2)	47 (25.3)	-	-	-	2.16	1.37 - 3.41	0.001
Experience raising children	343 (79.0)	205 (82.7)	138 (74.2)	-	-	-	1.96	1.10 - 3.47	0.021

Hib: *Haemophilus influenza* type b; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; Ref.: reference

Non-adjusted analysis: logistic regression analysis; Multivariable analysis: multiple logistic regression analysis adjusted with above variables.

PCV vaccine

Characteristics of PCPs were stratified by recommendation of the PCV vaccine and association between awareness of a PCV vaccine public subsidy and vaccination recommendation (Table 2). Overall, 314 (72.4%) PCPs reported awareness of a public subsidy and 235 (54.2%) recommended the vaccine. Physicians who reported awareness were significantly more likely to recommend vaccination than those who were not aware (non-adjusted analysis: OR 8.03, 95% CI 4.84–13.32, $p<0.001$; multivariable analysis: AOR 4.96, 95% CI 2.89–8.53, $p<0.001$). A higher proportion of pediatric patients and of PCPs with experience raising children were positively associated with vaccination recommendation, and higher PGY was inversely associated (Table 4).

Table 4. Association between primary care physicians' characteristics and recommendation of 7-valent pneumococcal conjugate vaccine

n=434

	Recommendation for PCV, n (%)			Non-adjusted analysis			Multivariable analysis		
Variable	Total, n=434	Recommen-dation (+), n=235	Recommen-dation (-), n=199	OR	95% CI	*p* value	AOR	95% CI	*p* value
Awareness of public subsidy for PCV	315 (72.6)	211 (89.8)	104 (52.3)	8.03	4.84 - 13.32	<0.001	4.96	2.89 - 8.53	<0.001
Full subsidy	369 (85.0)	194 (82.6)	175 (87.9)	-	-	-	0.62	0.33 - 1.17	0.14
Male	367 (84.6)	194 (82.6)	173 (86.9)	-	-	-	0.98	0.52 - 1.83	0.94
Postgraduate year：3-10	90 (20.7)	66 (28.1)	24 (12.1)	-	-	-	Ref.		
11-40	318 (73.3)	158 (67.2)	160 (80.4)	-	-	-	0.29	0.15 - 0.56	<0.001
>=41	26 (6.0)	11 (4.7)	15 (7.5)	-	-	-	0.18	0.06 - 0.54	0.002
Pediatric patients >=10%	174 (40.1)	127 (54.0)	47 (23.6)	-	-	-	2.5	1.57 - 3.98	<0.001
Experience raising children	343 (79.0)	197 (83.8)	146 (73.4)	-	-	-	2.61	1.43 - 4.74	0.002

PCV: 7-valent pneumococcal conjugate vaccine; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; Ref.: reference; Non-adjusted analysis: logistic regression analysis; Multivariable analysis: multiple logistic regression analysis adjusted with above variables.

HPV vaccine

Characteristics of PCPs stratified by recommendation of the HPV vaccine and the association between the awareness of an HPV vaccine public subsidy and vaccination recommendation are presented (Table 2). We found that 389 (89.6%) PCPs reported awareness of the public subsidy and 252 (58.1%) recommended the vaccine. Physicians who reported awareness were significantly more likely to recommend vaccination than those who were not aware (non-adjusted analysis: OR 5.03, 95% CI 2.47–10.24, p<0.001; multivariable analysis: AOR 4.17, 95% CI 2.00–8.70, p<0.001). Experience raising children was positively associated with recommendation, and higher PGY was inversely associated (Table 5).

Table 5. Association between primary care physicians' characteristics and recommendation of human papillomavirus vaccine

n=434

	Recommendation for HPV vaccine, n (%)			Non-adjusted analysis			Multivariable analysis		
Variable	Total, n=434	Recommen-dation (+), n=252	Recommen-dation (-), n=182	OR	95% CI	*p* value	AOR	95% CI	*p* value
Awareness of public subsidy for HPV vaccine	389 (89.6)	241 (95.6)	148 (81.3)	5.03	2.47 - 10.24	<0.001	4.17	2.00 - 8.70	<0.001
Full subsidy	385 (88.7)	225 (89.3)	160 (87.9)	-	-	-	1.25	0.66 - 2.35	0.49
Male	367 (84.6)	210 (83.3)	157 (86.3)	-	-	-	0.96	0.54 - 1.72	0.9
Postgraduate year：3-10	90 (20.7)	61 (24.2)	29 (15.9)	-	-	-	Ref.		
11-40	318 (73.3)	174 (69.1)	144 (79.1)	-	-	-	0.47	0.27 - 0.82	0.008
>=41	26 (6.0)	17 (6.8)	9 (5.0)	-	-	-	0.72	0.27 - 1.97	0.53
Pediatric patients >=10%	174 (40.1)	112 (44.4)	62 (34.1)	-	-	-	1.34	0.88 - 2.03	0.17
Experience raising children	343 (79.0)	211 (83.7)	132 (72.5)	-	-	-	2.21	1.31 - 3.72	0.003

HPV: human papillomavirus; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio, Ref.: reference; Non-adjusted analysis; logistic regression analysis; Multivariable analysis; multiple logistic regression analysis adjusted with above variables.

Sensitivity analysis

The sensitivity analysis included re-categorized outcomes for recommendation of vaccines. The results demonstrated that for each vaccine, PCPs who reported awareness of a subsidy were significantly more likely to recommend vaccination than those who were not aware: AOR 3.52 (95% CI 1.91–6.49, p<0.001) for the Hib vaccine, 4.42 (95% CI 2.45–7.98, p<0.001) for the PCV vaccine, and 5.08 (95% CI 2.29–11.25, p<0.001) for the HPV vaccine.

Discussion

This is the first investigation focused on the proportion of PCPs who have awareness of vaccination subsidies and their recommendations of Hib, PCV, and HPV vaccines, and the association between awareness of such subsidies and recommendation of vaccination. We found a positive association between physicians' awareness of the subsidy and their recommendation of vaccination.

These vaccines were recently introduced in Japan; Hib in 2008, PCV in 2010, bivalent HPV vaccine in 2009, and quadrivalent HPV vaccine in 2011. Gathering of data for this study was conducted in 2012, meaning the results reflect the actual clinical situation after new introduction of vaccines among PCPs in Japan. Our study showed that even among PCPs who administered childhood vaccinations, not all were aware that subsidies existed, and not all actively recommended vaccination. Vaccination fees serve as a

barrier to vaccination for patients,[9] and PCPs need access to information about vaccine costs, especially with regard to public subsidies. Of the three vaccines studied, the HPV vaccine was most commonly recognized by the surveyed PCPs. This was also the most expensive of these vaccines, and health care professionals have cited financial concerns as a barrier to vaccination.[27] It therefore appears PCPs need to be more aware of available subsidies for this vaccination.

However, the proportions of PCPs' recommendations were similar for all three vaccines. These proportions were low when compared with those in other countries; for instance, 68% of family physicians in the United States adopted recommendations for PCV vaccination in 2001, 1 year after the Centers for Disease Control and Prevention recommended it.[22] In 2008, 50% of the family physicians who administered the HPV vaccine in the United States strongly recommended the vaccine for girls aged 11–12 years, and 85% for girls aged 13–15 years.[23] However, studies conducted in 2011 reported that 40.0% of physicians (family physicians, pediatricians, and obstetricians/gynecologists) in the United States always recommended HPV vaccination, as did 45.6% of general practitioners in France.[28 29] Although the proportion of PCP recommendations of vaccination may differ by country and time of year, recommendations from healthcare providers are important for patients, especially with regard to new vaccine.[30]

For all three vaccines studied, there was a statistically significant association between PCPs' awareness of a public subsidy and their recommendation of vaccination. In comparing PCPs who had no

awareness of subsidies with those who were aware, the AOR for recommendation was 4.21 for the Hib vaccine, 4.96 for the PCV vaccine, and 4.17 for the HPV vaccine (Tables 3–5). These results suggest awareness is an important factor behind vaccination recommendation. The robustness of our results was demonstrated in sensitivity analysis using another method of re-categorization. Recent studies have highlighted that the cost of vaccination is also a barrier for physicians to recommend vaccination.[31 32] Multiple logistic regression analysis showed that, in addition to awareness, a higher proportion of pediatric patients was positively associated with recommendation of Hib and PCV vaccination, and experience raising children was positively associated with recommendation of all three vaccines (Tables 3–5). These results suggest provision of information or experience with children on a regular basis may affect PCPs' recommendations. We also found that a higher PGY number was inversely associated with recommendation (Tables 3–5). The Hib, PCV, and HPV vaccines were recently introduced in Japan, and PCPs with a lower PGY number may have greater interest in or knowledge about these vaccines because of their more recent education or training. This suggests providing information about public subsidies to older PCPs may be more effective than providing information to younger PCPs. A study conducted after introduction of the Hib vaccine in the United States reported younger physicians were more accepting of the vaccine than older ones; this supports our results.[33]

Our study also suggested PCPs' awareness of public subsidies, their having more pediatric patients, and their having experience raising children were important factors in increasing their recommendations

of childhood vaccination. For voluntary vaccinations without public subsidies, governmental introduction of a public subsidy may play an important role in increasing coverage.[9 32 34] For vaccinations already subsidized, implementing a plan to inform PCPs about the subsidy and providing PCPs with updated education and information about the vaccine and subsidy system (considering physician characteristics, especially age and those with fewer pediatric patients) may increase the proportion that recommend vaccination.

This study did have some limitations. First, there was a potential non-responder bias due to the low response rate. The proportion of younger PCPs (PGYs 3–10) was higher among responders in this study than in the target population (Table 1); therefore, PCPs who more actively promoted vaccination may have been more likely to respond. The actual levels of PCPs' awareness and recommendations may be lower. Second, factors such as knowledge about vaccination, including vaccine safety and effectiveness, PCPs' circumstances or abilities, and PCPs' experience may have affected their recommendation behavior.[29] We did not investigate PCPs' knowledge of vaccine safety and effectiveness; therefore, the association between their knowledge of vaccines and their vaccination recommendation behavior should be investigated in a future study.[32] To account for this limitation, we limited our analysis to PCPs who administered childhood vaccinations and we adjusted for the proportion of pediatric patients (factors related to PCPs' medical care circumstances and abilities). As is a general limitation of observational studies, we did not evaluate the effect of unknown confounding factors. Finally, although the study

participants were physician members of the JPCA, the largest society for PCPs in Japan, generalizability of the results for PCPs outside of Japan was unclear. Vaccination policy in Japan also changed after this study was conducted,[9 35]; therefore, an inter-annual survey is needed to accurately comprehend the current situation of vaccination among PCPs.

Conclusions

In this study, we described the proportion of PCPs' awareness of existence of public subsidies and their recommendations for the Hib, PCV, and HPV vaccines, and revealed a significant association between awareness and recommendation. Even among PCPs who administered childhood vaccinations, there was variability in these two areas. Our results suggest that informing PCPs about public subsidies may increase their recommendations for these vaccines and improve vaccination coverage.

Acknowledgements

We thank members of the Vaccine Project Team, Japan Primary Care Association (Tadao Okada, Akinari Moriya, Toshio Naito, Koji Ishibashi, Manabu Toyama, Kuniko Nakayama, Rei Suganaga, Takara Mori, and Jiro Takeuchi) for implementing this survey; Izumi Maruyama, President of the Japan Primary Care Association, and head office staff for their corporation in collecting and delivering the questionnaire; all physicians who took part in the survey; and staff of the Medical Community Support Institute, Saga

University (Tsuyoshi Kurata, Yoshio Hisata, Yukiko Yoshioka, Chiemi Hirotaki, and Riyo Fukumori) for their contributions to this study. We also thank Adam Goulston, MS, ELS, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

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Footnotes

Contributors: All authors declare they have contributed to this article. YS conducted the questionnaire, designed and implemented the survey, and performed analysis and interpretation of the data. YY performed analysis and interpretation of the data and critical revisions. MH conducted the questionnaire, designed the study, and performed critical revisions. NF conducted the questionnaire and performed interpretation of the data and critical revisions. TK arranged for the sampling and critical revisions. KT performed interpretation of the data and critical revisions. TS conducted the questionnaire and performed interpretation of the data and critical revisions. The Japan Primary Care Association Vaccine Project Team implemented the survey and performed critical revisions. SF performed interpretation of the data and critical revisions. All authors read and approved this manuscript version for submission.

Funding: This study was supported by a research grant for Research on Emerging and Re-emerging Infectious Diseases, Health and Labour Science Research Grants from the Ministry of Health, Labour and Welfare of Japan (H23-SHINKO-IPPAN-017), and a Clinical Research Grant from St. Luke's Life Science Institute.

Competing interests: None declared.

Patient consent: Obtained

Ethical approval: This study protocol was approved by the Institutional Review Board of Saga University Hospital (2012-05-13) and the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (E2528).

Provenance and peer review: Not commissioned; externally peer reviewed

Data sharing statement: No additional data are available.

Figure legend

Figure 1. Study flow

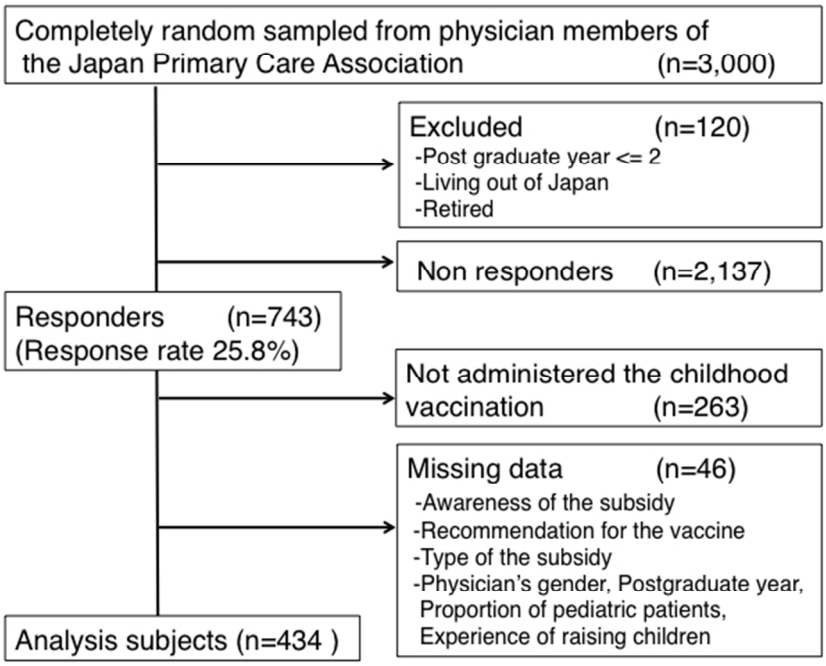

Figure 1. Study flow

254x190mm (72 x 72 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	-
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10-11, 29
		(b) Give reasons for non-participation at each stage	10-11, 29
		(c) Consider use of a flow diagram	29
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11
		(b) Indicate number of participants with missing data for each variable of interest	29

Outcome data	15*	Report numbers of outcome events or summary measures	12-18
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-18
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	19
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	22-23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-23
Generalisability	21	Discuss the generalisability (external validity) of the study results	22-23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	28

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Public subsidies and the recommendation of child vaccines among primary care physicians: a nationwide study in Japan

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-020923.R1
Article Type:	Research
Date Submitted by the Author:	06-Apr-2018
Complete List of Authors:	Sakanishi, Yuta; Saga Daigaku - Nabeshima Campus, Community Medical Support Institute, Faculty of Medicine Yamamoto, Yosuke; Kyoto University, Department of Healthcare Epidemiology Hara, Megumi; Saga Daigaku - Nabeshima Campus, Department of Preventive Medicine, Faculty of Medicine Fukumori, Norio; Saga Daigaku - Nabeshima Campus, Community Medical Support Institute, Faculty of Medicine Goto, Yoshihito; Kyoto University, Department of Healthcare Epidemiology Kusaba, Tesshu; The Hokkaido Centre for Family Medicine Tanaka, Keitaro; Saga Daigaku - Nabeshima Campus, Department of Preventive Medicine, Faculty of Medicine Sugioka, Takashi; Saga Daigaku - Nabeshima Campus, Community Medical Support Institute, Faculty of Medicine Japan Primary Care Association, Vaccine Project Team; Japan Primary Care Association Fukuhara, Shunichi; Kyoto University, Department of Healthcare Epidemiology
Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Health policy
Keywords:	PRIMARY CARE, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Paediatric infectious disease & immunisation < PAEDIATRICS, PREVENTIVE MEDICINE, PUBLIC HEALTH

TITLE PAGE

Public subsidies and the recommendation of child vaccines among primary care physicians: a nationwide study in Japan

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Word count: 3,162 words

ABSTRACT

Objectives

Although public subsidies and physician recommendations for vaccination play key roles in increasing childhood vaccination coverage, the association between them remains uncertain. This study aimed to identify the association between awareness of public subsidies and recommendations for *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (PCV), and human papillomavirus (HPV) vaccinations, among primary care physicians in Japan.

Design

Cross-sectional study

Setting

In 2012, a questionnaire was distributed among 3,000 randomly selected physicians who were members of the Japan Primary Care Association.

Participants

From the questionnaire, participants were limited to physicians who administered childhood vaccinations.

Primary and Secondary Outcome Measures

The primary measures were participants' awareness of public subsidies and their recommendation levels for Hib, PCV, and HPV vaccines. Multiple logistic regression analysis was performed to investigate the

association between awareness and recommendation, with adjustment for possible confounders.

Results

The response rate was 25.8% (743/2,880). Of 743 physician respondents, 434 were included as analysis subjects. The proportions that recommended vaccinations were 57.1% for Hib, 54.2% for PCV, and 58.1% for HPV. For each vaccine, multivariable analyses showed physicians who were aware of the subsidy were more likely to recommend vaccination than those who were not aware: the adjusted odds ratios were 4.21 (95% confidence interval [CI] 2.47–7.15) for Hib, 4.96 (95% CI 2.89–8.53) for PCV, and 4.17 (95% CI 2.00–8.70) for HPV.

Conclusions

Primary care physicians' awareness of public subsidies was found to be associated with their recommendations for the Hib, PCV, and HPV vaccines. Provision of information about public subsidies to these physicians may increase their likelihood to recommend vaccination.

Strengths and limitations of this study

- This is the first study to focus on the association between awareness of primary care physicians (PCPs) concerning vaccination subsidies and those PCPs' recommendations for vaccinations for children.
- Through multivariable analysis, we explored characteristics of PCPs who were associated with less vaccination recommendation; this may provide important information on how to increase such recommendations and vaccination coverage.
- One limitation was the low response rate, which may have caused non-responder bias.
- Another limitation was that the results' generalizability for PCPs outside of Japan was unclear.

MAIN TEXT

Introduction

Vaccination has proven to be a successful and cost-effective health intervention in preventive care.[1] Vaccination against *Haemophilus influenzae* type b (Hib) is a successful example. In the United States, introduction of the Hib vaccine reduced incidence of invasive Hib disease by 99%,[2] while in Kenya, a 93% decline was seen following vaccination.[3] Therefore, many childhood vaccines (including Hib) are routinely provided, especially in higher-income countries, where coverage is relatively high.[4-8]

In Japan, however, many important vaccines, including Hib, *Streptococcus pneumoniae* (7-valent pneumococcal conjugate vaccine: PCV), and human papillomavirus (HPV) were voluntary rather than routine. These vaccines were introduced in Japan in the following years: Hib in 2008, PCV in 2010, and bivalent HPV in 2009. There were no public subsidies for them at the time they were initially offered. Without public subsidies, patients must pay an out-of-pocket fee, and this cost burden may serve as a barrier to receiving vaccination.[9] Routine vaccinations are defined by the Preventive Vaccination Law and scheduled in the National Immunization Program. These vaccinations are not mandatory, though the Government of Japan strongly recommends them. In principle, vaccinations are administered individually, mainly funded by the national and local governments, and free of charge to recipients at private or public facilities at the request of the local government.[9 10] Coverage of traditional, routine

vaccinations (e.g., those for diphtheria, tetanus, and measles) is high, and their associated diseases are well-controlled.[9 11 12] However, coverage of voluntary vaccinations is much lower.[9] The Hib vaccine, for example, was first introduced to Japan in 2008 on a voluntary basis, and had estimated coverage of 5%–10% in 2010.[13] Therefore, the Government of Japan implemented subsidies for local governments for Hib, PCV, and HPV vaccine fees from November 2010, all at the same time.[14] The subsidies were intended for all children aged over 2 months and under 5 years for Hib and PCV, and all girls aged 12–16 years for HPV.[15] Local governments determined the subsidy amounts. All local governments have now started providing public subsidies for these three vaccines.

It is generally accepted that recommendation of vaccination, to children and their parents by a physician, is important for increasing coverage.[14 16-19] Primary care physicians (PCPs) provide care for all ages, from children to older people, and play a key role in childhood vaccination as vaccine providers, as well as pediatricians. However, no previous studies have examined PCPs' level of awareness of public subsidies for childhood vaccines in Japan, and the association between this awareness and recommendations for vaccination. Therefore, this study aimed to examine this association among PCPs in Japan for the Hib, PCV, and HPV vaccinations.

Methods

Study design, setting, and population

This study used a cross-sectional design with data drawn from a questionnaire conducted by the Japan Primary Care Association (JPCA), the largest academic association for PCPs in Japan. The survey was conducted in September–November 2012. In total, 3,000 physicians were randomly selected from among the 5,977 JPCA physician members. Selection was made using a random number list. Subject participants were then selected from among these 3,000 physicians in accordance with inclusion and exclusion criteria. The inclusion criteria were: physicians who were JPCA members and who administered childhood vaccination (defined as those who administered at least one of the Hib, PCV, and HPV vaccines in daily medical practice). Exclusion criteria were physicians who were retired or living out of Japan or within 2 years of their postgraduate year, as the latter group are classified as "junior residents" in Japan. Questionnaire items were based on previous studies.[16 17 19-28] We used a self-administered, anonymous questionnaire design and collected data on the participating PCPs' main practice category, practice setting (clinic, hospital, or other), local government of the practice, population under jurisdiction of the local government, and experience as a kindergarten or other school physician. Questionnaires were sent to each participant by postal mail. Additional details are given below.

Patient and Public Involvement

We obtained written informed consent from all participants before we conducted the survey. Public was not involved in this study. The study protocol was approved by the Institutional Review Board of Saga

University Hospital (2012-05-13) and the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (E2528).

Main exposure

The main exposure of this study was physicians' awareness of the existence of local government public subsidies for the target vaccine (awareness of public subsidy). For each vaccine, respondents were asked "Does the local government of your place of practice subsidize the vaccination?" Response options were "Yes," "No," and "I don't know." Answers of "Yes" were defined as "awareness of public subsidy." Answers of "No" or "I don't know" were defined as "no awareness of public subsidy."

Main outcome

The main outcome of this study was PCPs' active recommendation of a target vaccine to children and the children's parents in daily medical practice ("recommendation"). For each vaccine, respondents were asked "How do you recommend a target vaccine to vaccinees and their parents?" Response options, on a Likert-type scale, were: "Always recommend," "Maybe recommend," "No opinion," "Not recommend actively," and "Not recommend." Answers of "Always recommend" were defined as "recommendation." "Maybe recommend," "No opinion," "Not recommend actively," and "Not recommend" were defined as "no recommendation."

Possible confounders

Possible confounders were the physician's sex, postgraduate year, a proportion of pediatric patients (pediatric patients in the total patient population) that was high (≥10%) or low (<10%), and experience raising children as a parent. We added in these data from the questionnaire and also used public information held by the local government to investigate the type of the subsidy (full subsidy or not) for the three vaccines for each participant.

Statistical analyses

Logistic regression analysis was performed for each target vaccine (Hib, PCV, and HPV) to investigate the association between PCPs' awareness of a public subsidy for the target vaccine and their recommendation of that vaccine. Then, multiple logistic regression analysis was performed to investigate the association between awareness and recommendation, adjusting for possible confounders (full subsidy or not, physician's sex, postgraduate year, proportion of pediatric patients, and experience raising children).

The analysis subjects were set after excluding participants with missing data for the main exposure, main outcome, and possible confounders (mentioned above).

All statistical analyses used two-tailed tests of significance, with significance set at 0.05. Analyses

were performed with Stata/SE 13.1 (StataCorp LLC, College Station, TX, USA). Sensitivity analysis was performed for each vaccine using another method of re-categorization to reflect the dichotomization of the dependent variable (recommendation), with the response option "Maybe recommend" included in "recommendation."

Results

Study flow and demographics

Of the 3,000 randomly selected PCPs, 120 were excluded based on the inclusion and exclusion criteria, leaving a sample of 2,880. We received responses from 743 PCPs, for a response rate of 25.8%. The respondents were from all 47 prefectures of Japan. Of these respondents, 480 (64.6%) administered childhood vaccinations. We analyzed data for 434 (58.4%) after excluding 46 (6.2%) with missing data for covariates (Figure 1). The majority of these PCPs were men, postgraduate year 11–40, reported a clinical category of primary care, reported their practice setting as clinic, and had experience raising children (Table 1).

Table 1. Participants' characteristics

Characteristic	Analysis subjects n=434	Responders n=743	All physician members† n=5,977
	n (%)	n (%)	n (%)
Gender: male	367 (84.6%)	624 (84.0%)	5,071 (84.8%)
Postgraduate year：3-10	90 (20.7%)	153 (20.6%)	664 (11.1%)
11-40	318 (73.3%)	527 (71.0%)	4,248 (71.1%)
>=41	26 (6.0%)	62 (8.4%)	769 (12.9%)
Main practice category: primary care	358 (82.5%)	556 (74.8%)	-
Practice setting; clinic	307 (70.7%)	388 (52.3%)	-
Pediatric patients >=10%	174 (40.1%)	186 (26.2%)	-
Population of local government >= 50,000	277 (64.0%)	527 (71.5%)	-
Experience of kindergarten or other school physician	284 (65.4%)	403 (54.2%)	-
Experience raising children	343 (79.0%)	568 (76.5%)	-

†Physician members of the Japan Primary Care Association as of September 2012.

Main practice category: primary care: Answered main practice category as family physician or general practitioner or hospitalist/general physician; Pediatric patients: proportion of pediatric patients in the total patient population.

Hib vaccine

Characteristics of PCPs were stratified by recommendation of the Hib vaccine and the association between awareness of an Hib vaccine public subsidy and vaccination recommendation (Table 2). We

found 327 (75.3%) PCPs reported awareness of a public subsidy and 248 (57.1%) recommended the vaccine. PCPs who reported awareness were significantly more likely to recommend the vaccine than those who were not aware (non-adjusted analysis: OR 6.18, 95% confidence interval [CI] 3.77–10.12, p<0.001; multivariable analysis: adjusted odds ratio [AOR] 4.21, 95% CI 2.47–7.15, p<0.001). A higher proportion of pediatric patients and of PCPs with experience raising children were positively associated with recommendation. However, a higher postgraduate year was inversely associated (Table 3).

Table 2. Primary care physicians' awareness of public subsidies and recommendation levels for the Haemophilus influenzae type b vaccine, 7-valent pneumococcal conjugate vaccine, and human papillomavirus vaccine

n=434

Awareness of public subsidy for each vaccine	Total, n (%)	Recommendation level for each vaccine, n (%)				
		Always Recommend	Maybe Recommend	No opinion	Not recommend actively	Not Recommend
Hib vaccine						
Awareness (+)	327 (75.3%)	221 (67.6%)	78 (23.9%)	23 (7.0%)	3 (0.9%)	2 (0.6%)
Awareness (-)	107 (24.7%)	27 (25.2%)	40 (37.4%)	27 (25.2%)	8 (7.5%)	5 (4.7%)
Total	434 (100%)	248 (57.1%)	118 (27.2%)	50 (11.5%)	11 (2.5%)	7 (1.6%)
PCV vaccine						
Awareness (+)	315 (72.6%)	211 (67.0%)	77 (24.4%)	22 (7.0%)	4 (1.3%)	1 (0.3%)
Awareness (-)	119 (27.4%)	24 (20.2%)	45 (37.8%)	36 (30.3%)	8 (6.7%)	6 (5.0%)
Total	434 (100%)	235 (54.1%)	122 (28.1%)	58 (13.4%)	12 (2.8%)	7 (1.6%)
HPV vaccine						
Awareness (+)	389 (89.6%)	241 (62.0%)	121 (31.1%)	19 (4.9%)	6 (1.5%)	2 (0.5%)
Awareness (-)	45 (10.4%)	11 (24.4%)	18 (40.0%)	13 (28.9%)	3 (6.7%)	0 (0%)
Total	434 (100%)	252 (58.1%)	139 (32.0%)	32 (7.4%)	9 (2.1%)	2 (0.5%)

Hib: *Hemophilus influenzae* type b; PCV: 7-valent pneumococcal conjugate vaccine; HPV: human papillomavirus

Table 3. Association between primary care physicians' characteristics and recommendation of *Haemophilus influenzae* type b vaccine

n=434

Variable	Recommendation for Hib vaccine, n (%)			Non-adjusted analysis			Multivariable analysis		
	Total, n=434	Recommen-dation (+), n=248	Recommen-dation (-), n=186	OR	95% CI	p value	AOR	95% CI	p value
Awareness of public subsidy for Hib vaccine	327 (75.4%)	221 (89.1%)	106 (57.0%)	6.18	3.77 - 10.12	<0.001	4.21	2.47 - 7.15	<0.001
Full subsidy	371 (85.5%)	209 (84.3%)	162 (87.1%)	-	-	-	0.76	0.41 - 1.41	0.39
Male	367 (84.6%)	205 (82.7%)	162 (87.1%)	-	-	-	0.97	0.52 - 1.80	0.93
Postgraduate year：3-10	90 (20.7%)	68 (27.4%)	22 (11.8%)	-	-	-	Ref.		
11-40	318 (73.3%)	168 (67.7%)	150 (80.6%)	-	-	-	0.32	0.17 - 0.61	<0.001
>=41	26 (6.0%)	12 (4.8%)	14 (7.5%)	-	-	-	0.19	0.07 - 0.53	0.001
Pediatric patients >=10%	174 (40.1%)	127 (51.2%)	47 (25.3%)	-	-	-	2.16	1.37 - 3.41	0.001
Experience raising children	343 (79.0%)	205 (82.7%)	138 (74.2%)	-	-	-	1.96	1.10 - 3.47	0.021

Hib: *Haemophilus influenza* type b; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; Ref.: reference

Non-adjusted analysis: logistic regression analysis; Multivariable analysis: multiple logistic regression analysis adjusted with above variables.

PCV vaccine

Characteristics of PCPs were stratified by recommendation of the PCV vaccine and association between awareness of a PCV vaccine public subsidy and vaccination recommendation (Table 2). Overall, 315 (72.6%) PCPs reported awareness of a public subsidy and 235 (54.1%) recommended the vaccine. Physicians who reported awareness were significantly more likely to recommend vaccination than those who were not aware (non-adjusted analysis: OR 8.03, 95% CI 4.84–13.32, p<0.001; multivariable analysis: AOR 4.96, 95% CI 2.89–8.53, p<0.001). A higher proportion of pediatric patients and of PCPs with experience raising children were positively associated with vaccination recommendation, and higher postgraduate year was inversely associated (Table 4).

Table 4. Association between primary care physicians' characteristics and recommendation of 7-valent pneumococcal conjugate vaccine

n=434

Variable	Recommendation for PCV, n (%)			Non-adjusted analysis			Multivariable analysis		
	Total, n=434	Recommen-dation (+), n=235	Recommen-dation (-), n=199	OR	95% CI	*p* value	AOR	95% CI	*p* value
Awareness of public subsidy for PCV	315 (72.6%)	211 (89.8%)	104 (52.3%)	8.03	4.84 - 13.32	<0.001	4.96	2.89 - 8.53	<0.001
Full subsidy	369 (85.0%)	194 (82.6%)	175 (87.9%)	-	-	-	0.62	0.33 - 1.17	0.14
Male	367 (84.6%)	194 (82.6%)	173 (86.9%)	-	-	-	0.98	0.52 - 1.83	0.94
Postgraduate year：3-10	90 (20.7%)	66 (28.1%)	24 (12.1%)	-	-	-	Ref.		
11-40	318 (73.3%)	158 (67.2%)	160 (80.4%)	-	-	-	0.29	0.15 - 0.56	<0.001
>=41	26 (6.0%)	11 (4.7%)	15 (7.5%)	-	-	-	0.18	0.06 - 0.54	0.002
Pediatric patients >=10%	174 (40.1%)	127 (54.0%)	47 (23.6%)	-	-	-	2.5	1.57 - 3.98	<0.001
Experience raising children	343 (79.0%)	197 (83.8%)	146 (73.4%)	-	-	-	2.61	1.43 - 4.74	0.002

PCV: 7-valent pneumococcal conjugate vaccine; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; Ref.: reference; Non-adjusted analysis: logistic regression analysis; Multivariable analysis: multiple logistic regression analysis adjusted with above variables.

HPV vaccine

Characteristics of PCPs stratified by recommendation of the HPV vaccine and the association between the awareness of an HPV vaccine public subsidy and vaccination recommendation are presented (Table 2). We found that 389 (89.6%) PCPs reported awareness of the public subsidy and 252 (58.1%) recommended the vaccine. Physicians who reported awareness were significantly more likely to recommend vaccination than those who were not aware (non-adjusted analysis: OR 5.03, 95% CI 2.47–10.24, p<0.001; multivariable analysis: AOR 4.17, 95% CI 2.00–8.70, p<0.001). Experience raising children was positively associated with recommendation, and higher postgraduate year was inversely associated (Table 5).

Table 5. Association between primary care physicians' characteristics and recommendation of human papillomavirus vaccine

n=434

Variable	Recommendation for HPV vaccine, n (%)			Non-adjusted analysis			Multivariable analysis		
	Total, n=434	Recommen-dation (+), n=252	Recommen-dation (-), n=182	OR	95% CI	*p* value	AOR	95% CI	*p* value
Awareness of public subsidy for HPV vaccine	389 (89.6%)	241 (95.6%)	148 (81.3%)	5.03	2.47 - 10.24	<0.001	4.17	2.00 - 8.70	<0.001
Full subsidy	385 (88.7%)	225 (89.3%)	160 (87.9%)	-	-	-	1.25	0.66 - 2.35	0.49
Male	367 (84.6%)	210 (83.3%)	157 (86.3%)	-	-	-	0.96	0.54 - 1.72	0.9
Postgraduate year：3-10	90 (20.7%)	61 (24.2%)	29 (15.9%)	-	-	-	Ref.		
11-40	318 (73.3%)	174 (69.1%)	144 (79.1%)	-	-	-	0.47	0.27 - 0.82	0.008
>=41	26 (6.0%)	17 (6.8%)	9 (5.0%)	-	-	-	0.72	0.27 - 1.97	0.53
Pediatric patients >=10%	174 (40.1%)	112 (44.4%)	62 (34.1%)	-	-	-	1.34	0.88 - 2.03	0.171
Experience raising children	343 (79.0%)	211 (83.7%)	132 (72.5%)	-	-	-	2.21	1.31 - 3.72	0.003

HPV: human papillomavirus; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio, Ref.: reference; Non-adjusted analysis; logistic regression analysis; Multivariable analysis; multiple logistic regression analysis adjusted with above variables.

Sensitivity analysis

The sensitivity analysis included re-categorized outcomes for recommendation of vaccines. The results demonstrated that for each vaccine, PCPs who reported awareness of a subsidy were significantly more likely to recommend vaccination than those who were not aware: AOR 3.52 (95% CI 1.91–6.49, p<0.001) for the Hib vaccine, 4.42 (95% CI 2.45–7.98, p<0.001) for the PCV vaccine, and 5.08 (95% CI 2.29–11.25, p<0.001) for the HPV vaccine.

Discussion

This is the first investigation focused on the proportion of PCPs who have awareness of vaccination subsidies and their recommendations of Hib, PCV, and HPV vaccines, and the association between awareness of such subsidies and recommendation of vaccination. We found a positive association between physicians' awareness of the subsidy and their recommendation of vaccination.

These vaccines were recently introduced in Japan; Hib in 2008, PCV in 2010, bivalent HPV vaccine in 2009, and quadrivalent HPV vaccine in 2011. The subsidies for these three vaccines were implemented from November 2010. When subsidies were offered, information about them was conveyed to patients/families and providers though public outlets such as local government websites or public relations magazines. Additionally, public health nurses informed parents at the time the children received health check-ups. Local governments also sent notices about the subsidies to each medical facility and medical

association. Gathering of data for this study was conducted in 2012, meaning the results reflect the actual clinical situation after new introduction of vaccines among PCPs in Japan. The estimated coverage rates for these vaccines in 2012, were 70%–90% for Hib,[29 30] 80%–90% for PCV,[29 31] and 65%–75% for HPV.[32 33] Our study showed that even among PCPs who administered childhood vaccinations, not all were aware that subsidies existed, and not all actively recommended vaccination. Vaccination fees serve as a barrier to vaccination for patients,[9] and PCPs need access to information about vaccine costs, especially with regard to public subsidies. Of the three vaccines studied, the HPV vaccine was most commonly recognized by the surveyed PCPs. This was also the most expensive of these vaccines, and health care professionals have cited financial concerns as a barrier to vaccination.[34] It therefore appears PCPs need to be more aware of available subsidies for this vaccination.

However, the proportions of PCPs' recommendations were similar for all three vaccines. These proportions were low when compared with those in other countries; for instance, 68% of family physicians in the United States adopted recommendations for PCV vaccination in 2001, 1 year after the Centers for Disease Control and Prevention recommended it.[24] In 2008, 50% of the family physicians who administered the HPV vaccine in the United States strongly recommended the vaccine for girls aged 11–12 years, and 85% for girls aged 13–15 years.[25] However, studies conducted in 2011 reported that 40.0% of physicians (family physicians, pediatricians, and obstetricians/gynecologists) in the United States always recommended HPV vaccination, as did 45.6% of general practitioners in France.[35 36]

Although the proportion of PCP recommendations of vaccination may differ by country and time of year, recommendations from healthcare providers are important for patients, especially with regard to new vaccine.[37]

For all three vaccines studied, there was a statistically significant association between PCPs' awareness of a public subsidy and their recommendation of vaccination. In comparing PCPs who had no awareness of subsidies with those who were aware, the AOR for recommendation was 4.21 for the Hib vaccine, 4.96 for the PCV vaccine, and 4.17 for the HPV vaccine (Tables 3–5). These results suggest awareness is an important factor behind vaccination recommendation. The robustness of our results was demonstrated in sensitivity analysis using another method of re-categorization. Recent studies have highlighted that the cost of vaccination is also a barrier for physicians to recommend vaccination.[38 39] Multiple logistic regression analysis showed that, in addition to awareness, a higher proportion of pediatric patients was positively associated with recommendation of Hib and PCV vaccination, and experience raising children was positively associated with recommendation of all three vaccines (Tables 3–5). These results suggest provision of information or experience with children on a regular basis may affect PCPs' recommendations. We also found that a higher postgraduate year was inversely associated with recommendation (Tables 3–5). The Hib, PCV, and HPV vaccines were recently introduced in Japan, and PCPs with a lower postgraduate year may have greater interest in or knowledge about these vaccines because of their more recent education or training. This suggests providing information about public

subsidies to older PCPs may be more effective than providing information to younger PCPs. A study conducted after introduction of the Hib vaccine in the United States reported younger physicians were more accepting of the vaccine than older ones; this supports our results.[40]

Our study also suggested PCPs' awareness of public subsidies, their having more pediatric patients, and their having experience raising children were important factors in increasing their recommendations of childhood vaccination. For voluntary vaccinations without public subsidies, governmental introduction of a public subsidy may play an important role in increasing coverage.[9 39 41] For vaccinations already subsidized, implementing a plan to inform PCPs about the subsidy and providing PCPs with updated education and information about the vaccine and subsidy system (considering physician characteristics, especially age and those with fewer pediatric patients) may increase the proportion that recommend vaccination.

This study did have some limitations. First, there was a potential non-responder bias due to the low response rate. The proportion of younger PCPs (postgraduate year 3–10) was higher among responders in this study than in the target population (Table 1); therefore, PCPs who more actively promoted vaccination may have been more likely to respond. The actual levels of PCPs' awareness and recommendations may be lower. Second, factors such as knowledge about vaccination, including vaccine safety and effectiveness, PCPs' circumstances or abilities, and PCPs' experience may have affected their recommendation behavior.[36] We did not investigate PCPs' knowledge of vaccine safety

and effectiveness; therefore, the association between their knowledge of vaccines and their vaccination recommendation behavior should be investigated in a future study.[39] To account for this limitation, we limited our analysis to PCPs who administered childhood vaccinations and we adjusted for the proportion of pediatric patients (factors related to PCPs' medical care circumstances and abilities). As is a general limitation of observational studies, we did not evaluate the effect of unknown confounding factors. Finally, although the study participants were physician members of the JPCA, the largest society for PCPs in Japan, generalizability of the results for PCPs outside of Japan was unclear. Vaccination policy in Japan also changed after this study was conducted,[9 10]; therefore, an inter-annual survey is needed to accurately comprehend the current situation of vaccination among PCPs.

Conclusions

In this study, we described the proportion of PCPs' awareness of existence of public subsidies and their recommendations for the Hib, PCV, and HPV vaccines, and revealed a significant association between awareness and recommendation. Even among PCPs who administered childhood vaccinations, there was variability in these two areas. Our results suggest that informing PCPs about public subsidies may increase their recommendations for these vaccines and improve vaccination coverage.

Acknowledgements

We thank members of the Vaccine Project Team, Japan Primary Care Association (Tadao Okada, Akinari Moriya, Toshio Naito, Koji Ishibashi, Manabu Toyama, Kuniko Nakayama, Rei Suganaga, Takara Mori, and Jiro Takeuchi) for implementing this survey; Izumi Maruyama, President of the Japan Primary Care Association, and head office staff for their corporation in collecting and delivering the questionnaire; all physicians who took part in the survey; and staff of the Medical Community Support Institute, Saga University (Tsuyoshi Kurata, Yoshio Hisata, Yukiko Yoshioka, Chiemi Hirotaki, and Riyo Fukumori) for their contributions to this study. We also thank Adam Goulston, MS, ELS, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

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Footnotes

Contributors: All authors declare they have contributed to this article. YS conducted the questionnaire, designed and implemented the survey, and performed analysis and interpretation of the data. YY performed analysis and interpretation of the data and critical revisions. MH conducted the questionnaire, designed the study, and performed critical revisions. NF conducted the questionnaire and performed interpretation of the data and critical revisions. YG performed interpretation of the data and critical revisions. TK arranged for the sampling and critical revisions. KT performed interpretation of the data and critical revisions. TS conducted the questionnaire and performed interpretation of the data and critical revisions. The Japan Primary Care Association Vaccine Project Team implemented the survey and performed critical revisions. SF performed interpretation of the data and critical revisions. All authors read and approved this manuscript version for submission.

Funding: This study was supported by a research grant for Research on Emerging and Re-emerging Infectious Diseases, Health and Labour Science Research Grants from the Ministry of Health, Labour and Welfare of Japan (H23-SHINKO-IPPAN-017), and a Clinical Research Grant from St. Luke's Life Science Institute.

Competing interests: None declared.

Patient consent: Obtained

Ethical approval: This study protocol was approved by the Institutional Review Board of Saga University Hospital (2012-05-13) and the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (E2528).

Provenance and peer review: Not commissioned; externally peer reviewed

Data sharing statement: No additional data are available.

Figure legend

Figure 1. Study flow

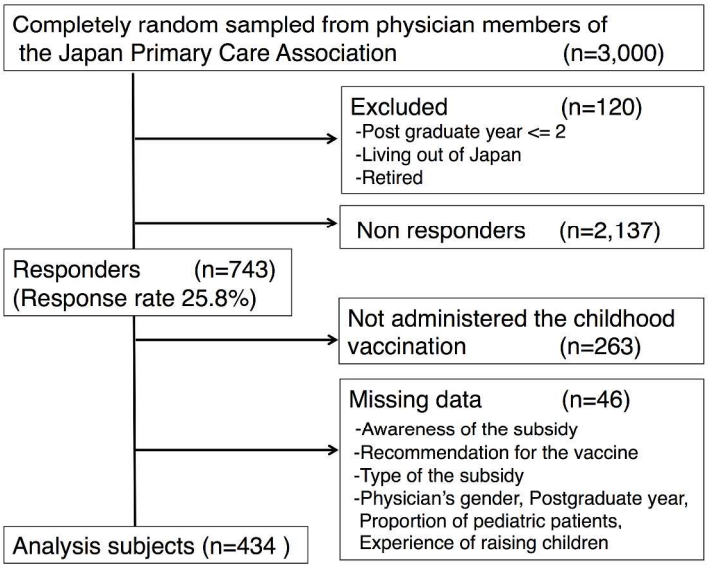

Figure 1.

297x209mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	-
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10-11, 29
		(b) Give reasons for non-participation at each stage	10-11, 29
		(c) Consider use of a flow diagram	29
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11
		(b) Indicate number of participants with missing data for each variable of interest	29

Outcome data	15*	Report numbers of outcome events or summary measures	12-18
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-18
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	19
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	22-23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-23
Generalisability	21	Discuss the generalisability (external validity) of the study results	22-23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	28

*Give information separately for exposed and unexposed groups.

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BMJ Open

Public subsidies and the recommendation of child vaccines among primary care physicians: a nationwide cross-sectional study in Japan

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-020923.R2
Article Type:	Research
Date Submitted by the Author:	28-May-2018
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Primary Subject Heading:	General practice / Family practice
Secondary Subject Heading:	Health policy
Keywords:	PRIMARY CARE, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Paediatric infectious disease & immunisation < PAEDIATRICS, PREVENTIVE MEDICINE, PUBLIC HEALTH

TITLE PAGE

Public subsidies and the recommendation of child vaccines among primary care physicians: a nationwide cross-sectional study in Japan

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Word count: 2,860 words

ABSTRACT

Objectives

Although public subsidies and physician recommendations for vaccination play key roles in increasing childhood vaccination coverage, the association between them remains uncertain. This study aimed to identify the association between awareness of public subsidies and recommendations for *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* (PCV), and human papillomavirus (HPV) vaccinations, among primary care physicians in Japan.

Design

Cross-sectional study

Setting

In 2012, a questionnaire was distributed among 3,000 randomly selected physicians who were members of the Japan Primary Care Association.

Participants

From the questionnaire, participants were limited to physicians who administered childhood vaccinations.

Primary and Secondary Outcome Measures

The primary measures were participants' awareness of public subsidies and their recommendation levels for Hib, PCV, and HPV vaccines. Multiple logistic regression analysis was performed to investigate the

association between awareness and recommendation, with adjustment for possible confounders.

Results

The response rate was 25.8% (743/2,880). Of 743 physician respondents, 434 were included as analysis subjects. The proportions that recommended vaccinations were 57.1% for Hib, 54.1% for PCV, and 58.1% for HPV. For each vaccine, multivariable analyses showed physicians who were aware of the subsidy were more likely to recommend vaccination than those who were not aware: the adjusted odds ratios were 4.21 (95% confidence interval [CI] 2.47–7.15) for Hib, 4.96 (95% CI 2.89–8.53) for PCV, and 4.17 (95% CI 2.00–8.70) for HPV.

Conclusions

Primary care physicians' awareness of public subsidies was found to be associated with their recommendations for the Hib, PCV, and HPV vaccines. Provision of information about public subsidies to these physicians may increase their likelihood to recommend vaccination.

Strengths and limitations of this study

- This is the first study to focus on the association between awareness of primary care physicians (PCPs) concerning vaccination subsidies and those PCPs' recommendations for vaccinations for children.
- To explore characteristics of PCPs found associated with less vaccination recommendation, multivariable logistic regression analysis was performed with background factors such as the physician's postgraduate year, proportion of pediatric patients, and experience raising children as a parent.
- Though participants were randomly selected, one limitation was non-responder bias, which was due to the PCPs' voluntary participation in the survey.
- Another limitation was that the results' generalizability for PCPs outside of Japan was unclear.

MAIN TEXT

Introduction

Vaccination has proven to be a successful and cost-effective health intervention in preventive care.[1] Vaccination against *Haemophilus influenzae* type b (Hib) is a successful example. In the United States, introduction of the Hib vaccine reduced incidence of invasive Hib disease by 99%,[2] while in Kenya, a 93% decline was seen following vaccination.[3] Therefore, many childhood vaccines (including Hib) are routinely provided, especially in higher-income countries, where coverage is relatively high.[4-8]

In Japan, however, many important vaccines, including Hib, *Streptococcus pneumoniae* (7-valent pneumococcal conjugate vaccine: PCV), and human papillomavirus (HPV) were voluntary rather than routine, and voluntary vaccinations were not covered by the National Immunization Program, without subsidies by the Government of Japan.[9] These vaccines were introduced in Japan in the following years: Hib in 2008, PCV in 2010, and bivalent HPV in 2009. There were no public subsidies for them at the time they were initially offered. Without public subsidies, patients must pay an out-of-pocket fee, and this cost burden may serve as a barrier to receiving vaccination.[9] Routine vaccinations are defined by the Preventive Vaccination Law and scheduled in the National Immunization Program. These vaccinations are not mandatory, though the Government of Japan strongly recommends them. In principle, vaccinations are administered individually, mainly funded by the national and local governments, and

free of charge to recipients at private or public facilities at the request of the local government.[9 10] Coverage of traditional, routine vaccinations (e.g., those for diphtheria, tetanus, and measles) is high, and their associated diseases are well-controlled.[9 11 12] However, coverage of voluntary vaccinations is much lower and some diseases those vaccinations target are endemic in the population.[9 12] The Hib vaccine, for example, was first introduced to Japan in 2008 on a voluntary basis, and had estimated coverage of 5%–10% in 2010.[13] Therefore, the Government of Japan implemented subsidies for local governments for Hib, PCV, and HPV vaccine fees from November 2010, all at the same time.[14] The subsidies were intended for all children aged over 2 months and under 5 years for Hib and PCV, and all girls aged 12–16 years for HPV.[15] Local governments determined the subsidy amounts. All local governments have now started providing public subsidies for these three vaccines.

It is generally accepted that recommendation of vaccination, to children and their parents by a physician, is important for increasing coverage.[14 16-19] Primary care physicians (PCPs) provide care for all ages, from children to older people, and play a key role in childhood vaccination as vaccine providers, as well as pediatricians. However, no previous studies have examined PCPs' level of awareness of public subsidies for childhood vaccines in Japan, and the association between this awareness and recommendations for vaccination. Therefore, this study aimed to examine this association among PCPs in Japan for the Hib, PCV, and HPV vaccinations.

Methods

Study design, setting, and population

This study used a cross-sectional design with data drawn from a questionnaire conducted by the Japan Primary Care Association (JPCA), the largest academic association for PCPs in Japan. The majority of the JPCA physician members were internists working as PCPs at a clinic or hospital. The survey was conducted in September–November 2012. In total, 3,000 physicians were randomly selected from among the 5,977 JPCA physician members. Selection was made using a random number list. Subject participants were then selected from among these 3,000 physicians in accordance with inclusion and exclusion criteria. The inclusion criteria were: physicians who were JPCA members and who administered childhood vaccination (defined as those who administered at least one of the Hib, PCV, and HPV vaccines in daily medical practice). Exclusion criteria were physicians who were retired or living out of Japan or within 2 years of their postgraduate year, as the latter group are classified as "junior residents" in Japan. Questionnaire items were based on previous studies.[16 17 19-28] We used a self-administered, anonymous questionnaire design and collected data on the participating PCPs' main practice category, practice setting (clinic, hospital, or other), local government of the practice, population under jurisdiction of the local government, and experience as a kindergarten or other school physician. Questionnaires were sent to each participant by postal mail. Additional details are given below.

Patient and Public Involvement

Patients and other members of the public were not involved in this study.

Main exposure

The main exposure of this study was physicians' awareness of the existence of local government public subsidies for the target vaccine (awareness of public subsidy). For each vaccine, respondents were asked "Does the local government of your place of practice subsidize the vaccination?" Response options were "Yes," "No," and "I don't know." Answers of "Yes" were defined as "awareness of public subsidy." Answers of "No" or "I don't know" were defined as "no awareness of public subsidy."

Main outcome

The main outcome of this study was PCPs' active recommendation of a target vaccine to children and the children's parents in daily medical practice ("recommendation"). For each vaccine, respondents were asked "How do you recommend a target vaccine to vaccinees and their parents?" Response options, on a Likert-type scale, were: "Always recommend," "Maybe recommend," "No opinion," "Not recommend actively," and "Not recommend." Answers of "Always recommend" were defined as "recommendation." "Maybe recommend," "No opinion," "Not recommend actively," and "Not recommend" were defined as "no recommendation."

Possible confounders

Possible confounders were the physician's sex, postgraduate year, a proportion of pediatric patients (pediatric patients in the total patient population) that was high (≥10%) or low (<10%), and experience raising children as a parent. We added in these data from the questionnaire and also used public information held by the local government to investigate the type of the subsidy (full subsidy or not) for the three vaccines for each participant.

Statistical analyses

Logistic regression analysis was performed for each target vaccine (Hib, PCV, and HPV) to investigate the association between PCPs' awareness of a public subsidy for the target vaccine and their recommendation of that vaccine. Then, multiple logistic regression analysis was performed to investigate the association between awareness and recommendation, adjusting for possible confounders (full subsidy or not, physician's sex, postgraduate year, proportion of pediatric patients, and experience raising children).

The analysis subjects were set after excluding participants with missing data for the main exposure, main outcome, and possible confounders (mentioned above).

All statistical analyses used two-tailed tests of significance, with significance set at 0.05. Analyses

were performed with Stata/SE 13.1 (StataCorp LLC, College Station, TX, USA). Sensitivity analysis was performed for each vaccine using another method of re-categorization to reflect the dichotomization of the dependent variable (recommendation), with the response option "Maybe recommend" included in "recommendation."

We obtained written informed consent from all participants before we conducted the survey. The study protocol was approved by the Institutional Review Board of Saga University Hospital (2012-05-13) and the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (E2528).

Results

Study flow and demographics

Of the 3,000 randomly selected PCPs, 120 were excluded based on the inclusion and exclusion criteria, leaving a sample of 2,880. We received responses from 743 PCPs, for a response rate of 25.8%. The respondents were from all 47 prefectures of Japan. Of these respondents, 480 (64.6%) administered childhood vaccinations. We analyzed data for 434 (58.4%) after excluding 46 (6.2%) with missing data for covariates (Figure 1). The majority of these PCPs were men, postgraduate year 11–40, reported a clinical category of primary care, reported their practice setting as clinic, and had experience raising children (Table 1).

Table 1. Participants' characteristics

Characteristic	Analysis subjects n=434	Responders n=743	All physician members† n=5,977
	n (%)	n (%)	n (%)
Gender: male	367 (84.6%)	624 (84.0%)	5,071 (84.8%)
Postgraduate year：3-10	90 (20.7%)	153 (20.6%)	664 (11.1%)
11-40	318 (73.3%)	527 (71.0%)	4,248 (71.1%)
>=41	26 (6.0%)	62 (8.4%)	769 (12.9%)
Main practice category: primary care	358 (82.5%)	556 (74.8%)	-
Practice setting; clinic	307 (70.7%)	388 (52.3%)	-
Pediatric patients >=10%	174 (40.1%)	186 (26.2%)	-
Population of local government >= 50,000	277 (64.0%)	527 (71.5%)	-
Experience of kindergarten or other school physician	284 (65.4%)	403 (54.2%)	-
Experience raising children	343 (79.0%)	568 (76.5%)	-

†Physician members of the Japan Primary Care Association as of September 2012.

Main practice category: primary care: Answered main practice category as family physician or general practitioner or hospitalist/general physician; Pediatric patients: proportion of pediatric patients in the total patient population.

Hib vaccine

Characteristics of PCPs were stratified by recommendation of the Hib vaccine and the association between awareness of an Hib vaccine public subsidy and vaccination recommendation (Table 2). We

found 327 (75.3%) PCPs reported awareness of a public subsidy and 248 (57.1%) recommended the vaccine. PCPs who reported awareness were significantly more likely to recommend the vaccine than those who were not aware (non-adjusted analysis: OR 6.18, 95% confidence interval [CI] 3.77–10.12, p<0.001; multivariable analysis: adjusted odds ratio [AOR] 4.21, 95% CI 2.47–7.15, p<0.001). A higher proportion of pediatric patients and of PCPs with experience raising children were positively associated with recommendation. However, a higher postgraduate year was inversely associated (Table 3).

Table 2. Primary care physicians' awareness of public subsidies and recommendation levels for the Haemophilus influenzae type b vaccine, 7-valent pneumococcal conjugate vaccine, and human papillomavirus vaccine

n=434

Awareness of public subsidy for each vaccine	Total, n (%)	Recommendation level for each vaccine, n (%)				
		Always Recommend	Maybe Recommend	No opinion	Not recommend actively	Not Recommend
Hib vaccine						
Awareness (+)	327 (75.3%)	221 (67.6%)	78 (23.9%)	23 (7.0%)	3 (0.9%)	2 (0.6%)
Awareness (-)	107 (24.7%)	27 (25.2%)	40 (37.4%)	27 (25.2%)	8 (7.5%)	5 (4.7%)
Total	434 (100%)	248 (57.1%)	118 (27.2%)	50 (11.5%)	11 (2.5%)	7 (1.6%)
PCV vaccine						
Awareness (+)	315 (72.6%)	211 (67.0%)	77 (24.4%)	22 (7.0%)	4 (1.3%)	1 (0.3%)
Awareness (-)	119 (27.4%)	24 (20.2%)	45 (37.8%)	36 (30.3%)	8 (6.7%)	6 (5.0%)
Total	434 (100%)	235 (54.1%)	122 (28.1%)	58 (13.4%)	12 (2.8%)	7 (1.6%)
HPV vaccine						
Awareness (+)	389 (89.6%)	241 (62.0%)	121 (31.1%)	19 (4.9%)	6 (1.5%)	2 (0.5%)
Awareness (-)	45 (10.4%)	11 (24.4%)	18 (40.0%)	13 (28.9%)	3 (6.7%)	0 (0%)
Total	434 (100%)	252 (58.1%)	139 (32.0%)	32 (7.4%)	9 (2.1%)	2 (0.5%)

Hib: *Hemophilus influenzae* type b; PCV: 7-valent pneumococcal conjugate vaccine; HPV: human papillomavirus

Table 3. Association between primary care physicians' characteristics and recommendation of *Haemophilus influenzae* type b vaccine

n=434

Variable	Recommendation for Hib vaccine, n (%)			Non-adjusted analysis			Multivariable analysis		
	Total, n=434	Recommen-dation (+), n=248	Recommen-dation (-), n=186	OR	95% CI	p value	AOR	95% CI	p value
Awareness of public subsidy for Hib vaccine	327 (75.4%)	221 (89.1%)	106 (57.0%)	6.18	3.77 - 10.12	<0.001	4.21	2.47 - 7.15	<0.001
Full subsidy	371 (85.5%)	209 (84.3%)	162 (87.1%)	-	-	-	0.76	0.41 - 1.41	0.39
Male	367 (84.6%)	205 (82.7%)	162 (87.1%)	-	-	-	0.97	0.52 - 1.80	0.93
Postgraduate year：3-10	90 (20.7%)	68 (27.4%)	22 (11.8%)	-	-	-	Ref.		
11-40	318 (73.3%)	168 (67.7%)	150 (80.6%)	-	-	-	0.32	0.17 - 0.61	<0.001
>=41	26 (6.0%)	12 (4.8%)	14 (7.5%)	-	-	-	0.19	0.07 - 0.53	0.001
Pediatric patients >=10%	174 (40.1%)	127 (51.2%)	47 (25.3%)	-	-	-	2.16	1.37 - 3.41	0.001
Experience raising children	343 (79.0%)	205 (82.7%)	138 (74.2%)	-	-	-	1.96	1.10 - 3.47	0.021

Hib: *Haemophilus influenza* type b; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; Ref.: reference

Non-adjusted analysis: logistic regression analysis; Multivariable analysis: multiple logistic regression analysis adjusted with above variables.

PCV vaccine

Characteristics of PCPs were stratified by recommendation of the PCV vaccine and association between awareness of a PCV vaccine public subsidy and vaccination recommendation (Table 2). Overall, 315 (72.6%) PCPs reported awareness of a public subsidy and 235 (54.1%) recommended the vaccine. Physicians who reported awareness were significantly more likely to recommend vaccination than those who were not aware (non-adjusted analysis: OR 8.03, 95% CI 4.84–13.32, p<0.001; multivariable analysis: AOR 4.96, 95% CI 2.89–8.53, p<0.001). A higher proportion of pediatric patients and of PCPs with experience raising children were positively associated with vaccination recommendation, and higher postgraduate year was inversely associated (Table 4).

Table 4. Association between primary care physicians' characteristics and recommendation of 7-valent pneumococcal conjugate vaccine

n=434

Variable	Recommendation for PCV, n (%)			Non-adjusted analysis			Multivariable analysis		
	Total, n=434	Recommen-dation (+), n=235	Recommen-dation (-), n=199	OR	95% CI	*p* value	AOR	95% CI	*p* value
Awareness of public subsidy for PCV	315 (72.6%)	211 (89.8%)	104 (52.3%)	8.03	4.84 - 13.32	<0.001	4.96	2.89 - 8.53	<0.001
Full subsidy	369 (85.0%)	194 (82.6%)	175 (87.9%)	-	-	-	0.62	0.33 - 1.17	0.14
Male	367 (84.6%)	194 (82.6%)	173 (86.9%)	-	-	-	0.98	0.52 - 1.83	0.94
Postgraduate year：3-10	90 (20.7%)	66 (28.1%)	24 (12.1%)	-	-	-	Ref.		
11-40	318 (73.3%)	158 (67.2%)	160 (80.4%)	-	-	-	0.29	0.15 - 0.56	<0.001
>=41	26 (6.0%)	11 (4.7%)	15 (7.5%)	-	-	-	0.18	0.06 - 0.54	0.002
Pediatric patients >=10%	174 (40.1%)	127 (54.0%)	47 (23.6%)	-	-	-	2.5	1.57 - 3.98	<0.001
Experience raising children	343 (79.0%)	197 (83.8%)	146 (73.4%)	-	-	-	2.61	1.43 - 4.74	0.002

PCV: 7-valent pneumococcal conjugate vaccine; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; Ref.: reference; Non-adjusted analysis: logistic regression analysis; Multivariable analysis: multiple logistic regression analysis adjusted with above variables.

HPV vaccine

Characteristics of PCPs stratified by recommendation of the HPV vaccine and the association between the awareness of an HPV vaccine public subsidy and vaccination recommendation are presented (Table 2). We found that 389 (89.6%) PCPs reported awareness of the public subsidy and 252 (58.1%) recommended the vaccine. Physicians who reported awareness were significantly more likely to recommend vaccination than those who were not aware (non-adjusted analysis: OR 5.03, 95% CI 2.47–10.24, p<0.001; multivariable analysis: AOR 4.17, 95% CI 2.00–8.70, p<0.001). Experience raising children was positively associated with recommendation, and higher postgraduate year was inversely associated (Table 5).

Table 5. Association between primary care physicians' characteristics and recommendation of human papillomavirus vaccine

n=434

Variable	Recommendation for HPV vaccine, n (%)			Non-adjusted analysis			Multivariable analysis		
	Total, n=434	Recommen-dation (+), n=252	Recommen-dation (-), n=182	OR	95% CI	*p* value	AOR	95% CI	*p* value
Awareness of public subsidy for HPV vaccine	389 (89.6%)	241 (95.6%)	148 (81.3%)	5.03	2.47 - 10.24	<0.001	4.17	2.00 - 8.70	<0.001
Full subsidy	385 (88.7%)	225 (89.3%)	160 (87.9%)	-	-	-	1.25	0.66 - 2.35	0.49
Male	367 (84.6%)	210 (83.3%)	157 (86.3%)	-	-	-	0.96	0.54 - 1.72	0.9
Postgraduate year：3-10	90 (20.7%)	61 (24.2%)	29 (15.9%)	-	-	-	Ref.		
11-40	318 (73.3%)	174 (69.1%)	144 (79.1%)	-	-	-	0.47	0.27 - 0.82	0.008
>=41	26 (6.0%)	17 (6.8%)	9 (5.0%)	-	-	-	0.72	0.27 - 1.97	0.53
Pediatric patients >=10%	174 (40.1%)	112 (44.4%)	62 (34.1%)	-	-	-	1.34	0.88 - 2.03	0.171
Experience raising children	343 (79.0%)	211 (83.7%)	132 (72.5%)	-	-	-	2.21	1.31 - 3.72	0.003

HPV: human papillomavirus; Pediatric patients: proportion of pediatric patients in the total patient population; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio, Ref.: reference; Non-adjusted analysis; logistic regression analysis; Multivariable analysis; multiple logistic regression analysis adjusted with above variables.

Sensitivity analysis

The sensitivity analysis included re-categorized outcomes for recommendation of vaccines. The results demonstrated that for each vaccine, PCPs who reported awareness of a subsidy were significantly more likely to recommend vaccination than those who were not aware: AOR 3.52 (95% CI 1.91–6.49, p<0.001) for the Hib vaccine, 4.42 (95% CI 2.45–7.98, p<0.001) for the PCV vaccine, and 5.08 (95% CI 2.29–11.25, p<0.001) for the HPV vaccine.

Discussion

This is the first investigation focused on the proportion of PCPs who have awareness of vaccination subsidies and their recommendations of Hib, PCV, and HPV vaccines, and the association between awareness of such subsidies and recommendation of vaccination. We found a positive association between physicians' awareness of the subsidy and their recommendation of vaccination.

These vaccines were recently introduced in Japan; Hib in 2008, PCV in 2010, bivalent HPV vaccine in 2009, and quadrivalent HPV vaccine in 2011. The subsidies for these three vaccines were implemented from November 2010. When subsidies were offered, information about them was conveyed to patients/families and providers though public outlets such as local government websites or public relations magazines. Additionally, public health nurses informed parents at the time the children received health check-ups. Local governments also sent notices about the subsidies to each medical facility and medical

association. Gathering of data for this study was conducted in 2012, meaning the results reflect the actual clinical situation after new introduction of vaccines among PCPs in Japan. The estimated coverage rates for these vaccines in 2012, were 70%–90% for Hib,[29 30] 80%–90% for PCV,[29 31] and 65%–75% for HPV.[32 33] Our study showed that even among PCPs who administered childhood vaccinations, not all were aware that subsidies existed, and not all actively recommended vaccination. Vaccination fees serve as a barrier to vaccination for patients,[9] and PCPs need access to information about vaccine costs, especially with regard to public subsidies. Of the three vaccines studied, the HPV vaccine was most commonly recognized by the surveyed PCPs. This was also the most expensive of these vaccines, and health care professionals have cited financial concerns as a barrier to vaccination.[34] It therefore appears PCPs need to be more aware of available subsidies for this vaccination.

However, the proportions of PCPs' recommendations were similar for all three vaccines. These proportions were low when compared with those in other countries; for instance, 68% of family physicians in the United States adopted recommendations for PCV vaccination in 2001, 1 year after the Centers for Disease Control and Prevention recommended it.[24] In 2008, 50% of the family physicians who administered the HPV vaccine in the United States strongly recommended the vaccine for girls aged 11–12 years, and 85% for girls aged 13–15 years.[25] However, studies conducted in 2011 reported that 40.0% of physicians (family physicians, pediatricians, and obstetricians/gynecologists) in the United States always recommended HPV vaccination, as did 45.6% of general practitioners in France.[35 36]

Although the proportion of PCP recommendations of vaccination may differ by country and time of year, recommendations from healthcare providers are important for patients, especially with regard to new vaccine.[37]

For all three vaccines studied, there was a statistically significant association between PCPs' awareness of a public subsidy and their recommendation of vaccination. In comparing PCPs who had no awareness of subsidies with those who were aware, the AOR for recommendation was 4.21 for the Hib vaccine, 4.96 for the PCV vaccine, and 4.17 for the HPV vaccine (Tables 3–5). These results suggest awareness is an important factor behind vaccination recommendation. The robustness of our results was demonstrated in sensitivity analysis using another method of re-categorization. Recent studies have highlighted that the cost of vaccination is also a barrier for physicians to recommend vaccination.[38 39] Multiple logistic regression analysis showed that, in addition to awareness, a higher proportion of pediatric patients was positively associated with recommendation of Hib and PCV vaccination, and experience raising children was positively associated with recommendation of all three vaccines (Tables 3–5). These results suggest provision of information or experience with children on a regular basis may affect PCPs' recommendations. We also found that a higher postgraduate year was inversely associated with recommendation (Tables 3–5). The Hib, PCV, and HPV vaccines were recently introduced in Japan, and PCPs with a lower postgraduate year may have greater interest in or knowledge about these vaccines because of their more recent education or training. This suggests providing information about public

subsidies to older PCPs may be more effective than providing information to younger PCPs. A study conducted after introduction of the Hib vaccine in the United States reported younger physicians were more accepting of the vaccine than older ones; this supports our results.[40]

Our study also suggested PCPs' awareness of public subsidies, their having more pediatric patients, and their having experience raising children were important factors in increasing their recommendations of childhood vaccination. For voluntary vaccinations without public subsidies, governmental introduction of a public subsidy may play an important role in increasing coverage.[9 39 41] For vaccinations already subsidized, implementing a plan to inform PCPs about the subsidy and providing PCPs with updated education and information about the vaccine and subsidy system (considering physician characteristics, especially age and those with fewer pediatric patients) may increase the proportion that recommend vaccination.

This study did have some limitations. First, there was a potential non-responder bias due to the low response rate. The proportion of younger PCPs (postgraduate year 3–10) was higher among responders in this study than in the target population (Table 1); therefore, PCPs who more actively promoted vaccination may have been more likely to respond. The actual levels of PCPs' awareness and recommendations may be lower. Second, factors such as knowledge about vaccination, including vaccine safety and effectiveness, PCPs' circumstances or abilities, and PCPs' experience may have affected their recommendation behavior.[36] We did not investigate PCPs' knowledge of vaccine safety

and effectiveness; therefore, the association between their knowledge of vaccines and their vaccination recommendation behavior should be investigated in a future study.[39] To account for this limitation, we limited our analysis to PCPs who administered childhood vaccinations and we adjusted for the proportion of pediatric patients (factors related to PCPs' medical care circumstances and abilities). As is a general limitation of observational studies, we did not evaluate the effect of unknown confounding factors. Finally, although the study participants were physician members of the JPCA, the largest society for PCPs in Japan, generalizability of the results for PCPs outside of Japan was unclear. Vaccination policy in Japan also changed after this study was conducted,[9 10]; therefore, an inter-annual survey is needed to accurately comprehend the current situation of vaccination among PCPs.

Conclusions

In this study, we described the proportion of PCPs' awareness of existence of public subsidies and their recommendations for the Hib, PCV, and HPV vaccines, and revealed a significant association between awareness and recommendation. Even among PCPs who administered childhood vaccinations, there was variability in these two areas. Our results suggest that informing PCPs about public subsidies may increase their recommendations for these vaccines and improve vaccination coverage.

Acknowledgements

We thank members of the Vaccine Project Team, Japan Primary Care Association (Tadao Okada, Akinari Moriya, Toshio Naito, Koji Ishibashi, Manabu Toyama, Kuniko Nakayama, Rei Suganaga, Takara Mori, and Jiro Takeuchi) for implementing this survey; Izumi Maruyama, President of the Japan Primary Care Association, and head office staff for their corporation in collecting and delivering the questionnaire; all physicians who took part in the survey; and staff of the Community Medical Support Institute, Saga University (Tsuyoshi Kurata, Yoshio Hisata, Yukiko Yoshioka, Chiemi Hirotaki, and Riyo Fukumori) for their contributions to this study. We also thank Adam Goulston, MS, ELS, from Edanz Group (www.edanzediting.com/ac) for editing a draft of this manuscript.

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Footnotes

Contributors: All authors declare they have contributed to this article. YS conducted the questionnaire, designed and implemented the survey, and performed analysis and interpretation of the data. YY performed analysis and interpretation of the data and critical revisions. MH conducted the questionnaire, designed the study, and performed critical revisions. NF conducted the questionnaire and performed interpretation of the data and critical revisions. YG performed interpretation of the data and critical revisions. TK arranged for the sampling and critical revisions. KT performed interpretation of the data and critical revisions. TS conducted the questionnaire and performed interpretation of the data and critical revisions. The Japan Primary Care Association Vaccine Project Team implemented the survey and performed critical revisions. SF performed interpretation of the data and critical revisions. All authors read and approved this manuscript version for submission.

Funding: This study was supported by a research grant for Research on Emerging and Re-emerging Infectious Diseases, Health and Labour Science Research Grants from the Ministry of Health, Labour and Welfare of Japan (H23-SHINKO-IPPAN-017), and a Clinical Research Grant from St. Luke's Life Science Institute.

Competing interests: None declared.

Patient consent: Obtained

Ethical approval: This study protocol was approved by the Institutional Review Board of Saga University Hospital (2012-05-13) and the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (E2528).

Provenance and peer review: Not commissioned; externally peer reviewed

Data sharing statement: No additional data are available.

Figure legend

Figure 1. Study flow

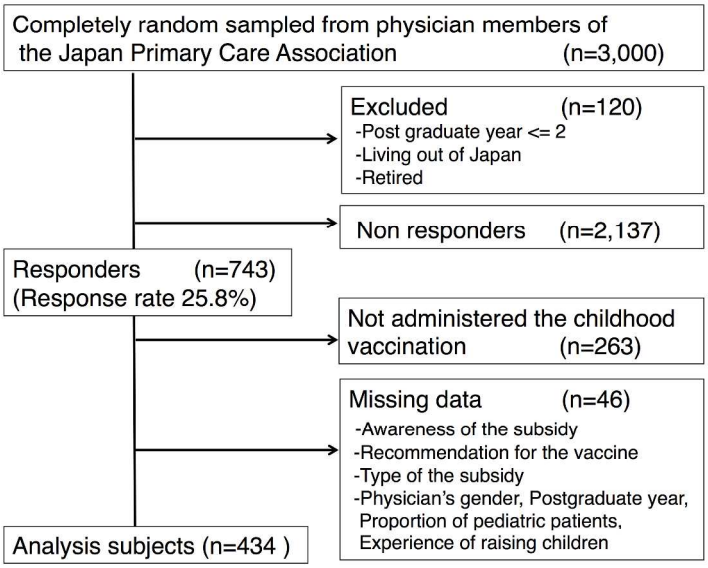

Figure 1.

297x209mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Reported on page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	-
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	-
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	-
		(*c*) Explain how missing data were addressed	10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7
		(*e*) Describe any sensitivity analyses	10
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10-11, 29
		(b) Give reasons for non-participation at each stage	10-11, 29
		(c) Consider use of a flow diagram	29
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11
		(b) Indicate number of participants with missing data for each variable of interest	29

Outcome data	15*	Report numbers of outcome events or summary measures	12-18
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-18
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	19
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	22-23
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-23
Generalisability	21	Discuss the generalisability (external validity) of the study results	22-23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	28

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.